REMARKS

Claims 39-44, 50, 56, 93, 102, 104, 110, and 111 have been amended.

Claims 17-116 are pending.

I. Amendments

The specification has been amended to replace language reciting, "(now allowed)" with language reciting, "(now U.S. Patent No. 6,284,486)."

Claims 39-44, 50, 56, 93, 102, 104, 110, and 111 have been amended to replace language reciting, "ATCC" with language reciting, "American Type Culture Collection." Claims 102 and 104 have been amended to replace language reciting, "encoded by" with language reciting, "contained in."

The amendments do not introduce new matter under 35 U.S.C. § 132. Therefore, entry of the amendments is respectfully requested.

II. Priority

The Examiner indicated that the continuation data on page 1 of the specification should be updated. Paper No. 11, page 3. Accordingly, the first sentence of the specification has been amended to replace language reciting, "(now allowed)" with language reciting, "(now U.S. Patent No. 6,284,486)." Thus, the priority data have been updated.

III. Information Disclosure Statement

The Examiner indicated that the Information Disclosure Statement mailed October 4, 2001 fails to comply with the provisions of 37 C.F.R. §§ 1.97, 1.98, and M.P.E.P. § 609 because no English translation was provided for reference AL1. As a result, reference AL1 was not considered on the merits. Applicants respectfully disagree and traverse.

A written translation of a foreign language document submitted for consideration in an Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98 is not a *per se*

requirement. 37 C.F.R. § 1.98(a)(3)(ii) indicates that applicants are required to provide a translation only "if a written English-language translation of a non-English-language document, or portion thereof, is within the possession, custody, or control of, or is readily available" to the applicant. M.P.E.P. § 609 subsection III.A(2) explains that "[i]f no translation is submitted, the examiner will consider the information in view of the concise explanation and insofar as it is understood on its face," which includes "English language abstracts." M.P.E.P. §609 III.A(2) (8th Ed. 2001). The M.P.E.P. further states that "[s]ubmission of an English language abstract of a reference may fulfill the requirement for a concise explanation." Id. at § 609 III.A(3). Because reference AL1 was submitted with an English-language abstract it was submitted in compliance with the provisions of 37 C.F.R. §§ 1.97, 1.98, and M.P.E.P. § 609 and should have been considered by the Examiner.

Applicants note that the Examiner found an English language equivalent application, Honjo, et al. and considered it in accordance with M.P.E.P. § 609(III)(A)(3), which provides that an "English-language equivalent application may be submitted to fulfill this requirement if it is, in fact, a translation of a foreign language application being listed in an information disclosure statement." However, this does not alter the fact that reference AL1, as submitted, complied with 37 C.F.R. §§ 1.97, 1.98, and M.P.E.P. § 609 and therefore should have been considered by the Examiner.

In view of the above, Applicants respectfully request that the Examiner reconsider reference AL1. For the Examiner's convenience, included herewith as Attachment A is a clean copy of page 1 of PTO form 1449 mailed October 4, 2001.

IV. Rejections Under 35 U.S.C. § 101

A. Utility of HOIPS I Polypeptides

The Examiner rejected claims 17-28, 30-36, 38-47, 49-53, 55-59, 61-74, 76-81, 83-90, 92-99, 101-107, 109-114, and 116 for lack of utility under 35 U.S.C. §101 on the grounds that "the claimed proteins are not supported by either a specific asserted utility or a well established utility." Paper No. 11, page 3. Specifically, the Examiner asserted:

> "the specification fails to assert any utility for the claimed proteins or the polynucleotides encoding these proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed proteins or the polynucleotides encoding them such that another non-asserted utility would be well-established."

Paper No. 11, pages 3-4. Applicants respectfully disagree and traverse.

All that is needed to satisfy the utility requirement under 35 U.S.C. § 101 is that the evidence be "reasonably predictive" of the asserted utility. Nelson v. Bowler, 626 F.2d 853, 856-57, 206 USPQ 881, 883-84 (C.C.P.A. 1980). All that is required is a reasonable correlation between the evidence and the asserted utility. M.P.E.P. §2107.03(III) at page 2100-44. Applicants need not provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." In re Irons, 340 F.2d 974, 978, 144 USPQ 351, 354 (C.C.P.A. 1965).

Contrary to the Examiner's suggestion, the specification discloses specific and substantial utilities of the claimed invention, such as the use of the claimed invention in cancer diagnosis and prognosis. For example, at page 26, lines 14-18, the specification teaches that mammals with cancer, particularly acute myelogenous leukemias, express significantly altered levels of the HOIPS I protein and mRNA encoding the HOIPS I protein as compared to a corresponding mammal of the same species without cancer. The specification discloses on page 27, lines 23-30, that the HOIPS I polypeptides of the invention may be used for the diagnosis of cell proliferative disorders including acute myelogenous leukemias, *e.g.* acute monocytic leukemia, acute myeloblastic leukemia, acute erythroleukemia, and acute undifferentiated leukemia. These diagnostic methods using HOIPS I may involve assaying the expression level of the HOIPS I protein in mammalian cells or body fluid, *e.g.*, sera, and comparing the protein expression level with a standard HOIPS I protein expression level. Specification, page 26, line 19. Such utilities are specific (not all genes can be used as markers for proliferative neoplasia) and substantial (advance detection of disease is a utility in a "real world" context). M.P.E.P. §2107.01(I) (8th Ed. 2001) at page 2100-32.

Moreover, the asserted HOIPS I utilities are reasonably correlated with HOIPS I data disclosed in the specification. For example, the specification teaches that HOIPS I has significant homology, about 45% identical and 64% similar, to the chicken MD-I

protein, a v-myb-responsive gene during myeloid expression. Specification, page 4, lines and 16-25, page 8, lines 13 16 and Figure 2. MD-1, a member of the unique set of genes within the myelomonocytic lineage, contributes to the unique differentiation phenotype displayed by both normal and transformed cells and is important for the onset of various cell proliferative disorders. Specification, page 4, lines 3-4 and 16-25. Burk et al. *J. EMBO* 10:3713-3719 (1991), submitted previously in this application as document AS1 in the IDS filed October 4, 2001, teaches that MD-I is a myb-regulated gene and that v-myb transforms myelomonocytic cells and induces them to acquire an immature state of differentiation. Thus, evidence for utility of the claimed invention as a marker for cell proliferative disorders is disclosed in the specification and a reasonable correlation is provided between the biological roles of HOIPS I and detection of a disease condition.

Even assuming *arguendo* that the biological function or activity of the HOIPS I protein has not been shown by Applicants, the asserted diagnostic utility of the claimed invention is still specific and substantial. Utility for the nucleic acids in a diagnostic method does not turn on whether there is knowledge of the particular function of HOIPS I. Only the levels of the gene or protein in a particular sample are examined for indicia of cell proliferative disorders; the specific activity of the gene is irrelevant. Thus, contrary to the Examiner's allegation, the specification disclosures a specific, substantial, and well-established utility for the claimed invention.

The Examiner also stated:

> the utility of a HOIPS I polypeptide encoded by a cDNA is not a substantial utility because there is no real world context in which to use a protein having no known activity. This situation requires carrying out future research to identify the activity of the protein or reasonably confirm a 'real world' context of use and therefore does not define substantial activity.

Paper No. 11, page 4. However, the asserted utilities are substantial because, as discussed *supra,* the HOIPS I polypeptides of the invention have activity and the function of the HOIPS I protein is made clear to one of ordinary skill in the art.

In addition, the specification teaches therapeutic uses of HOIPS I polypeptides for the treatment of cell proliferative diseases. Such therapeutic applications of HOIPS I polypeptides include, for example, the generation of an antagonistic antibody against

HOIPS I polypeptides. The specification teaches that "enhanced levels of the HOIPS I protein can be detected in certain body fluids (e.g., sera, plasma, urine and spinal fluid) from mammals with certain leukemias, e.g. acute myelogenous leukemia," indicating increased expression of HOIPS I polypeptides in leukemia. Specification, page 26, lines 18-20. It also teaches that HOIPS I antibodies can be administered to treat cell proliferative diseases in which there is increased expression of HOIPS I polypeptides, such as in the leukemias described *supra*. Specification, page 35, lines 9-11. Administration of antibodies generated against HOIPS I polypeptides to treat, for example, acute myelogenous leukemia, is a substantial and real world application of the claimed invention.

Utility exists for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." In re Brana, 51 F.3d 1560, 1568 (Fed. Cir. 1995). As discussed *supra*, the specification teaches the use of HOIPS I polypeptides in the diagnosis of cell proliferative disorders as well as therapeutic application of antibodies against HOIPS I polypeptides for the treatment of, for example acute myelogenous leukemia. Such diagnostic and therapeutic utilities are specific and substantial with real world applications immediately apparent to a skilled artisan and thereby satisfy the usefulness requirement without the need for further research.

The utilities asserted for the claimed HOIPS I polypeptides are specific, substantial, and credible. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 17-28, 30-36, 38-47, 49-53, 55-59, 61-74, 76-81, 83-90, 92-99, 101-107, 109-114, and 116 under 35 U.S.C. § 101 for lack of utility.

B. Claims to HOIPS I Fragments and Variants

The Examiner rejected claims directed to various fragments, conserved substitutions, mutants, variants, and compositions of the HOIPS I protein under 35 U.S.C.

§ 101 on the grounds that the specification does not describe functional properties of the entire protein or of the fragments, conserved substitutions, mutants, variants, and compositions thereof. Paper No. 11, page 5. Applicants respectfully disagree and traverse.

In the same manner that the specification discloses utility for the full-length HOIPS I protein, the specification discloses similar utilities for fragments, variants, and compositions of the HOIPS I protein. For example, the specification teaches that HOIPS I fragments and variants have "HOIPS I polypeptide activity." Specification, page 20, line 23. Moreover, the specification teaches that HOIPS I polypeptide fragments, variants, or compositions thereof can generate antibodies, elicit an antibody response, and can therefore be used for diagnostic purposes in the same manner as the full-length HOIPS I protein. Specification, page 24, lines 13-17, page 28 lines 10-21. Thus, the specification provides a specific, substantial, credible, and well established utility for the HOIPS I protein as well as for fragments, conserved substitutions, mutants, variants, and compositions thereof.

The Examiner also commented that it is "not clear from the description on page 19 about the heterologous protein structure, and/or its function." Paper No. 11, page 6. Applicants notice that this is not a formal rejection by the Examiner. The specification at page 19, lines 1-12, describes what a heterologous sequence is, provides examples as to what constitutes a heterologous polypeptide, as well as how to make and use a heterologous sequence in combination with the HOIPS I protein of the instant invention. As the specification describes, a heterologous sequence can be used *inter alia* to improve stability, facilitate purification, and to give rise to secretion and expression of the desired protein. See specification, page 19, lines 1-11. The addition of a heterologous sequence does not affect the asserted utility of the claimed HOIPS I polypeptides. Thus, the specification adequately and clearly describes HOIPS I polypeptides comprising heterologous sequences as well as how to use such sequences.

In sum, the specification asserts specific, substantial, credible, and well-established utilities for the claimed HOIPS I polypeptides as well as for fragments, variants, and compositions thereof, such as diagnosis of certain leukemias. As such, reconsideration and withdrawal of the rejection of claims 17-28, 30-36, 38-47, 49-53, 55-59, 61-74, 76-81,

83-90, 92-99, 101-107, 109-114, and 116 for lack of utility under 35 U.S.C. § 101 is respectfully requested.

VI. Enablement Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 17-28, 30-36, 38-47, 49-53, 55-59, 61-74, 76-81, 83-90, 92-99, 101-107, 109-114, and 116 for lack of enablement under 35 U.S.C. § 112, first paragraph, on the grounds that since the claimed invention is allegedly "not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Paper No. 11, page 6. Applicants respectfully disagree and traverse.

As discussed *supra*, the instant invention is supported by a specific, substantial, and credible asserted utility. As such, one skilled in the art would clearly know how to use the claimed invention. Accordingly, reconsideration and withdrawal of the rejection is requested.

The Examiner also rejected claims 39-44, 50, 56, 93, 102, 104, 110, and 111 and the dependent claims thereto for lack of utility because the "claims recite necessity of a deposited clone, ATCC 97825, and do not meet fully with the deposit requirements set." Paper No. 11, page 7. The Examiner indicates that "[s]ubmission of a copy of the receipt would overcome this rejection." *Id.* While Applicants believe that they have met the deposit requirements, a copy of the deposit receipt for Accession No. ATCC 97825 is submitted concurrently herewith as Attachment B. Accordingly, reconsideration and withdrawal of the rejection for lack of enablement under 35 U.S.C. § 112, first paragraph is respectfully requested.

VII. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 20-25, 32-33, 39-44, 50, 56, 62, 93, 102, 104, 110, and 111 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

Claims 39-44, 50, 56, 93, 102, 104, 110, and 111 have been amended to replace language reciting, "ATCC" with language reciting, "American Type Culture Collection."

Upon entry of the amendments requested herewith, Applicants submit that the indefiniteness rejection of claims 39-44, 50, 56, 93, 102, 104, 110, and 111 under 35 U.S.C. § 112, second paragraph is rendered moot.

Regarding claims 20-25, 32, 33, and 62(a), Applicants submit that they are definite as written. The claims refer to SEQ ID NO:2. The numbering of amino acid residues for SEQ ID NO:2 contains negative numbers. As described in the specification on page 6, lines 9-12, the negative numbers correspond to the first 20 residues of the sequence, which is the leader sequence. Thus, when viewed in its totality, the specification makes it clear that a negative number recited in reference to SEQ ID NO:2 corresponds to a particular residue of SEQ ID NO:2 as provided in the sequence listing. Accordingly, claims 20-25, 32, 33, and 62(a) are definite under 35 U.S.C. § 112.2.

Claims 102 and 104 have been amended to replace language reciting, "encoded by" with language reciting, "contained in." Upon entry of the amendments requested herewith, Applicants submit that the indefiniteness rejection of claims 102 and 104 under 35 U.S.C. § 112, second paragraph is rendered moot.

CONCLUSION

It is believed that no fees are required for entry of this response. However, if there are any fees due in connection with the filing of this paper, please charge the appropriate fees to our Deposit Account No. 08-3425.

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Respectfully submitted,

By _____

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